Enantioselective Syntheses of Monofunctionalized Deltacyclenes Using a [CoI_2/Zn] Catalytic System

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The homo Diels–Alder (HDA) reaction still remains the most powerful tool for the synthesis of tetracyclic compounds **3** called "*Deltacyclenes*",[1] starting from norbornadiene (NBD, **1**) and acetylenic compounds **2**.[2] In the metal-catalyzed version of the HDA reaction, two efficient catalytic systems have so far been used: [Co(acac)$_3$/Et_2AlCl/L], in which the cobalt active species are generated *in situ* by reduction of Co(acac)$_3$ with Et_2AlCl in the presence of chelating bisphosphines,[3–5] and [CoI_2/Zn/L], in which the cobalt salt, in the presence of 2 equiv of PPh_3,[6] is reduced *in situ* with zinc powder in suspension.

It has been demonstrated that high stereochemical control can be achieved in these [2 + 2 + 2] cycloadditions through the presence of catalytic amounts of appropriate chiral ligands with both catalytic systems. Highly enantioselective syntheses of monosubstituted deltacyclenes have been performed with the [Co(acac)$_3$/Et_2AlCl/L*][7–9] or [CoI_2/Zn/L*][10] catalytic systems from nonfunctionalized acetylenes such as phenylacetylene and 1-hexyne, respectively, by the use of chelating bisphosphines and aminophosphinephosphinite ligands (AMPP).[11] These catalytic systems are very sensitive to the anhydrous character of the cobalt species, the coordinating ability of the solvent, and the presence and position of functionalized groups on the monosubstituted acetylenes. The low reactivity of some functionalized alkynes has proven to be the major limitation to the homo Diels–Alder reaction,[12] since propargylic derivatives failed to react under the [Co(acac)$_3$/Et_2AlCl/L*] conditions.[5]

As a part of a program aimed at the synthesis of polycyclic natural compounds using transition metal catalysis, we planned to prepare two classes of compounds; deltacyclenes with an allylic acetate functionality, and deltacyclenols, which can be considered as potential precursors of tricyclic functionalized compounds.[13] In this paper, we wish to report an extension of the scope of the HDA reaction to 2-propyn-1-ol (**2a**, propargyl alcohol) and 3-butyn-1-ol (**2e**) and their ethers and esters (Figure 1). Derivatives of **2a** have previously been found to be unreactive substrates. We also report that these reactions are conveniently run enantioselectively. The cobalt-catalyzed HDA reactions between NBD and acetylenic compounds[14] **2** proceed smoothly in CH_2Cl_2 or $ClCH_2CH_2Cl$ at room temperature affording the expected tetracyclic compounds **3** (Table 1).

Although the reaction proceeds in a heterogeneous medium, stirring speed (entries 5–7) has no decisive influence on the yield. The concentration of the catalytic cobalt species plays a much more important role with functionalized dienophiles than with nonfunctionalized ones. At higher catalyst concentrations, the yields are greatly decreased (entries 1, 2; 4, 5; 8, 10; and 9, 11)

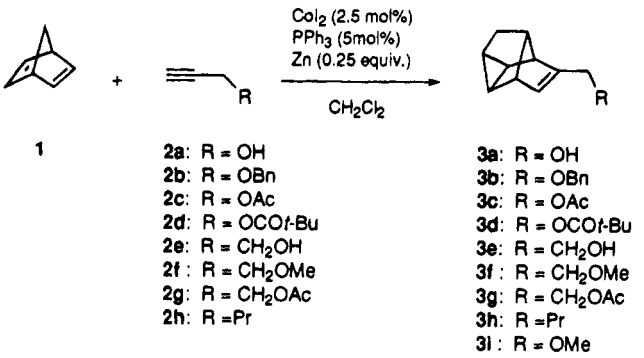

Figure 1.

Table 1. [2 + 2 + 2] Cycloaddition of NBD and Functionalized Alkynes Catalyzed by [CoI_2/PPh_3/Zn]

entry	alkyne	[CoI_2][a] (mol·L^{-1})	time (h)	yield[b] (%)
1	**2a**	0.041	12	45
2	**2a**	0.031	12	55
3	**2b**	0.041	12	25[c]
4	**2c**	0.031	12	60
5	**2c**	0.041	12	48
6	**2c**	0.041	12	47[d,f]
7	**2c**	0.041	12	46[e,f]
8	**2d**	0.031	12	53[f]
9	**2d**	0.031	12	58
10	**2d**	0.041	12	27[f]
11	**2d**	0.041	12	23
12	**2e**	0.041	4	87
13	**2e**	0.031	4	92
14	**2f**	0.041	3	97
15	**2g**	0.041	4	86[f]
16	**2g**	0.031	4	98[g]
17	**2g**	0.031	4	98[f,g]

[a] Molar ratio, unless otherwise noted, NBD/alkyne/Co/PPh_3/Zn = 40/40/1/2/10, CH_2Cl_2, temperature 21 ± 1 °C, stirring speed 800 rpm. [b] Isolated yield. [c] Same conversion was obtained with 3-methoxy-1-propyne at this temperature. [d] Stirring speed 600 rpm. [e] Stirring speed 400 rpm. [f] $ClCH_2CH_2Cl$ as solvent. [g] Molar ratio NBD/alkyne = 40/44.

(1) The name deltacyclane for tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane was first introduced by A. Nickon; Nickon, A.; Pandit, G. D.; Williams, R. O. *Tetrahedron Lett.* **1967**, 2851. For the origin of the name, see: Nickon, A.; Silverman, E. F. *Organic Chemistry. The Name Game*; Pergamon: New York, 1987; pp 216–217.

(2) Blomquist, A. T.; Meinwald, Y. C. *J. Am. Chem. Soc.* **1958**, *81*, 667.

(3) Lyons, J. E.; Myers, H. K.; Schneider, A. *J. Chem. Soc., Chem. Commun.* **1978**, 636.

(4) Lyons, J. E.; Myers, H. K.; Schneider, A. *Ann. N. Y. Acad. Sci.* **1980**, *333*, 273.

(5) Lautens, M.; Crudden, C. M. *Organometallics* **1989**, *8*, 2733.

(6) Duan, I.-F.; Cheng, C. H.; Shaw, J. S.; Cheng, S. S.; Liou, K. F. *J. Chem. Soc., Chem. Commun.* **1991**, 1347.

(7) Lautens, M.; Lautens, J. C.; Smith, A. C. *J. Am. Chem. Soc.* **1990**, *112*, 5627.

(8) Brunner, H.; Muschiol, M.; Prester, F. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 652.

(9) Brunner, H.; Prester, F. *J. Organomet. Chem.* **1991**, *414*, 401.

(10) Pardigon, O.; Buono, G. *Tetrahedron Asymmetry* **1993**, *4*, 1977.

(11) Mortreux, A.; Petit, F.; Buono, G.; Peiffer, G. *Bull. Soc. Chim. Fr.* **1987**, *4*, 631.

(12) Using the [Co(acac)$_3$/Et_2AlCl/L] catalytic system, Lautens has pointed out the lack of reactivity of propargylic ethers and esters which act as poison for other known HDA reactions.[4] The cycloaddition of methyl prop-2-ynyl ether with NBD catalyzed with the [CoI_2/Zn/L*] catalytic system only occurs under harsh conditions,[6] which are not suitable for asymmetric HDA reactions.

(13) Nickon, A.; Kwasnik, H. R.; Mathew, C. T.; Swartz, T. D.; Williams, R. O.; Di Giorgio, J. B. *J. Org. Chem.* **1978**, *43*, 3904. For instance, acid-catalyzed acetolysis of deltacyclane readily cleaves the cyclopropane ring to afford *exo*-4-brexyl acetate and *exo*-2-brendyl acetate, the proportion of the latter increases with time.

(14) Brandsma, L. *Preparative Acetylenic Chemistry*, 2nd ed.; Elsevier: New York, 1988.

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Table 2. Enantioselective Homo Diels–Alder Reactions Using (*S*)-(+)-ValNOP (4)

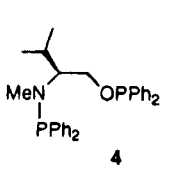
entry	alkyne	4/Co[a]	time (h)	yield[b] (%)	ee[c] (%)
1	**2a**	1	24	24	59.7[d]
2	**2c**	1	24	47	60.7
3	**2c**	2	24	53	78.2
4	**2d**	1	24	48	32.1
5	**2d**	2	24	45	36.4
6	**2e**	1	12	27	94.7[d]
7	**2e**	2	16	58	95.1[d]
8	**2g**	1	12	99	95.4
9	**2g**	2	16	87	95.6

[a] Molar ratio, unless otherwise noted, NBD/alkyne/Co/Zn = 40/40/1/10, in CH_2Cl_2 (6 mL), stirring speed 800 rpm, reaction temperature 10 °C. [b] Isolated yield. [c] Determinated at ±0.2% by GLC on modified β-cyclodextrine columns (see Experimental Section). [d] Ee was measured after conversion of alcohols **3a** and **3e** to the corresponding acetates **3c** and **3g**.

because the formation of aromatic compounds via trimerization of acetylenes becomes a major competitive reaction when using oxygen-substituted dienophiles. At the same time, deltacyclene formation rates with propargyl alcohol (**2a**) and its derivatives are much slower compared with those of phenylacetylene and 1-hexyne. Homologation to homopropargylic acetate **2g** allows the formation of HDA adduct **3g** more rapidly and in good yields. The chemical yield becomes nearly quantitative using a slight excess of acetylenic compound (entries 16, 17). Surprisingly, dienophiles **2a** and **2e**, bearing no hydroxyl protecting group, lead to deltacyclenols **3a** and **3e** in moderate to good yields, depending on the position of the acetylenic bond. Similar yields obtained with the corresponding ether **2b** or acetate **2c** prove that the catalytic cobalt species are not affected by the presence of protic species.

Propargyl compounds **2a**, **2b**, and **2c** react more slowly in the HDA with NBD than unfunctionalized acetylenic compounds, such as phenylacetylene or 1-hexyne (**2h**) and homopropargylic compounds **2e** and **2f**. However, in a competitive reaction between propargylic acetate (**2c**) and 1-hexyne (**2h**), the major cycloadduct **3c** results from the reaction of the NBD with the less reactive dienophile **2c**. This result is probably due to a selective affinity of the catalyst for **2c**, through coordination of the oxygen atom.

Highly enantioselective HDA reactions with oxygen-substituted dienophiles (prepared from oct-1-yn-8-ol) using the [$Co(acac)_3$/Et_2AlCl/L*] catalytic system have been reported by Lautens.[7] The reactions proceed only with alkyl-substituted acetylenes bearing a remote oxygen atom. Since enantioselective synthesis of deltacyclenes from propargylic and homopropargylic compounds has never been reported so far, we probed the AMPP ligand (*S*)-(+)-ValNOP (**4**), easily prepared in three steps from (*S*)-valine,[11] as a vector of chirality in the present system.



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The effect of the phosphine/cobalt ratio (L/Co) on enantioselectivity of the reaction has been studied (Table 2).

AMPP ligand **4** used in our catalyst system affords deltacyclenes in good enantiomeric excess (ee), as well as good chemical yields in agreement when PPh_3 is used as ligand (Table 1). A dramatic effect on the variation of the ee is observed with propargylic alcohol derivatives: changing the pivaloyl to an acetyl group increases the ee from 32 to 60% (entries 2, 4) and from 36 to 78% (entries 3, 5) depending on the L/Co ratio. Increasing the side chain length (homopropargylic compounds) also increases both chemical yields from 47 to 99% and the ee from 60 to 95% (entries 2, 8). Optically active deltacyclenols **3a** and **3e** were obtained with the same ee as those obtained from the corresponding esters to **2c** and **2g** but in lower chemical yields (entries 1, 2; 6, 8; and 7, 9).

Table 3. Influence of the Temperature at Different 4/Co Ratios on the ee of the HDA Reactions of NBD and Acetylenic Acetates 2c and 2g

entry	alkyne[a]	4/Co ratio	*T* (°C)	time (h)	yield[b] (%)	ee[c] (%)
1	**2g**	1	24	24	99	95.9
2	**2g**	1	10	12	95	95.4
3	**2g**	1	20	4	85	95.0
4	**2g**	1	25	3	83	94.4
5	**2g**	1	30	2	77	93.6
6	**2g**	2	0	24	99	95.4
7	**2g**	2	10	16	97	95.5
8	**2g**	2	20	8	88	95.6
9	**2g**	2	25	6	83	95.3
10	**2g**	2	29	4	74	95.0
11	**2c**	1	10	24	53	78.2
12	**2c**	1	20	18	50	78.0
13	**2c**	1	29	12	49	77.9
14	**2c**	2	10	24	15	60.7
15	**2c**	2	20	20	11	48.0
16	**2c**	2	29	17	10	35.5

[a] Molar ratio, unless otherwise noted, NBD/alkyne/Co/Zn = 40/40/1/10, in dry CH_2Cl_2 (6 mL), 800 rpm. [b] Isolated yield. [c] Determinated at ±0.2% by GLC on modified β-cyclodextrine columns (see Experimental Section).

The effect of the temperature at different 4/Co ratios on enantioselectivity of HDA reactions with dienophiles **2c** and **2g** has also been examined (Table 3).

In agreement with our previous results obtained in the enantioselective syntheses of *n*-butyl- and phenyldeltacyclenes using (*S*)-(+)-ValNOP (**4**),[10] we observed the same variation of chemical yields with temperature and the L/Co ratio.[15] With homopropargylic acetate **2g** differences are less important when the L/Co ratio increases from 1 to 2 compared to propargylic acetate **2c** and nonfunctionalized dienophiles.[16] The absolute configurations of cycloadducts **3a**, **3c**, **3e**, and **3g**, prepared from their corresponding propargylic and homopropargylic alcohols or acetates, have been determined according to the procedure used by Lautens.[7] Racemic and scalemic deltacyclenols **3a** and **3e** were transformed into the corresponding methyl ethers **3i** and **3f** and then submitted to hydroboration–oxidation to afford *exo* deltacyclanols **5a**, **6a** and **5b**, **6b** (Figure 2). The regioselectivity of the hydroboration–oxidation greatly depends on the nature of the R substituent, i.e., **5a/6a** = 85/15, **5b/6b** = 99/1. Conversion of **5a** and **6a** to their Mosher ester

(15) Optimal yields for the HDA using phenyl acetylene or 1-hexyne were obtained at ca. 10 °C. Increasing the reaction temperature also increases the rate of side reactions such as dimerization of NBD and trimerization of alkynes.

(16) The variation of ee with the temperature was more important with nonfunctionalized dienophiles such as 1-hexyne **2h** than with propargyl acetate **2c**, and best ee were obtained with a L/Co ratio = 2. This difference in reactivity may be attribute to a coordination of the oxygen atom to the cobalt, increasing the influence of the entropy term ($\Delta\Delta S^{\ddagger}$) in the free enthalpy ($\Delta\Delta G^{\ddagger}$) reaction. Unpublished results from our laboratory.

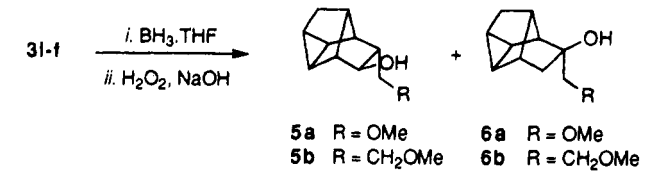

Figure 2.

derivatives[17] provides two diastereomeric compounds, the absolute configurations of which were assigned using the method first described by Mosher[17b] (see supplementary material). The four functionalized deltacyclenes **3a**, **3c**, **3e**, and **3f** obtained using (*S*)-(+)-ValNOP (**4**) as a chiral ligand have the same absolute configuration as (−)-*n*-butyldeltacyclene **3h** ((−)-(1*S*,2*R*,3*R*,4*R*,6*S*,7*R*)-8-*n*-butyltetracyclo[4.3.0.0^{2,4}.0^{3,7}]non-8-ene) prepared using the same ligand.[10] Optically active deltacyclenols **3a** and **3e** are also easily obtained in good yields from the corresponding acetates **3c** and **3g** by saponification (K_2CO_3, MeOH).

In summary, we report here the first successful cobalt-catalyzed HDA reactions of NBD and propargylic compounds[18] under mild conditions. Enantioselective catalysis using (*S*)-(+)-ValNOP (**4**), a bidentate organophosphorus ligand easily obtained from (S)-valine,[11] associated to a cobalt catalyst, promotes the homo Diels–Alder reaction, and depending on the nature of the acetylenic compound, high optical and chemical yields can be obtained. Studies on the transformation of deltacyclenes **3** into functionalized polycyclic compounds via rearrangement reactions are currently under investigation in our laboratory, and results will be reported in due course.

Experimental Section

General. All reactions were performed under an argon atmosphere. All solvents and reagents were purchased from commercial sources and were used without purification unless otherwise indicated. Dichloromethane and 1,2-dichloroethane were degassed with nitrogen before use. Acetylenic compounds **2b–d** and **2f–g** were prepared according to described procedures[14] from propargylic and homopropargylic alcohols and alkanoyl chlorides and were distilled before use. Chiral ligand (*S*)-(+)-ValNOP (**4**) was prepared according to ref 11. Silica gel (Merck, 70–230 or 230–400 mesh) was used for column chromatography. Thin layer chromatography (TLC) was performed on Merck silica gel 60-F254 (0.25 mm precoated on glass). Enantiomeric excesses were measured by gas chromatography using a 40-m Lipodex E (Heptakis (6-*O*-methyl-2,3-di-*O*-pentyl)-β-cyclodextrine) column, column temperature 90 °C, carrier gas He 0.55 bar; injection temperature 170 °C.[19]

Catalytic HDA Reactions: General Procedure. To a suspension of CoI_2 (78 mg, 0.25 mmol), triphenylphosphine (131 mg, 0.5 mmol), and Zn powder (163 mg, 2.5 mmol) in dry CH_2Cl_2 (6 mL) was added the alkyne (10 mmol) and NBD (921 mg, 10 mmol). The mixture was stirred at 21 ± 1 °C for a period indicated in Table 1, diluted with Et_2O (15 mL), and filtered through a Celite pad. The crude product was purified by medium pressure liquid chromatography (MPLC) on a silica gel column. For the asymmetric reaction listed in Table 2, **4** was substituted for the triphenylphosphine.

(17) (a) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Am. Chem. Soc.* **1969**, *34*, 2543. (b) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512. For a practical DCC esterification protocol see: Paquette, L. A.; Maynard, G. D. *J. Am. Chem. Soc.* **1992**, *114*, 5018.

(18) Intramolecular HDA reactions catalyzed by the [Co(acac)$_3$/Et$_2$AlCl/L*] catalytic system have been recently reported. See: Lautens, M.; Tamm, W.; Edwards, L. G. *J. Org. Chem.* **1992**, *57*, 8.

(19) In all cases, the dextrorotatory alkene was the major enantiomer obtained using (*S*)-(+)-ValNOP (**4**) and elutes in second position.

(1*R*,2*R*,3*R*,4*R*,6*S*,7*R*)-8-(Hydroxymethyl)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]non-8-ene (3a) was obtained as a pale yellow oil by MPLC (petroleum ether/Et_2O 90/10): yield 24% (99.7% purity by GC); $[\alpha]^{20}_{589}$ +0.4°, (*c* 2.0, CH_2Cl_2), ee 60%; IR (neat) ν 3410, 3055, 1449, 1026 cm^{-1}; ^{1}H NMR δ 1.29 (m, 2H), 1.52 (m, 2H), 1.70 (br s, 1H), 1.90 (br, OH), 1.97 (s, 1H), 2.57 (br s, 2H), 4.22 (s, 2H), 5.87 (s, 1H); ^{13}C NMR δ 22.6, 23.6, 25.9, 32.8, 48.5, 49.4, 57.5, 61.7, 129.5, 149.8. Anal. Calcd for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 81.09; H, 8.10.

(1*R,2*R**,3*R**,4*R**,6*S**,7*R**)-8-(Benzyloxymethyl)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]non-8-ene (3b)** was obtained as a colorless liquid by MPLC (petroleum ether/Et_2O 90/10): yield 25% (99.9% purity by GC); IR (neat) ν 3063, 2956, 1617, 1597, 1455, 1072, 1029 cm^{-1}; ^{1}H NMR δ 1.30 (m, 2H), 1.52 (m, 2H), 1.69 (m, 1H), 2.00 (m, 1H), 2.57 (m, 1H), 2.63 (m, 1H), 4.10 (d, *J* = 1.1 Hz, 2H), 4.48 (s, 2H), 5.95 (dd, *J* = 1.1, 2.8 Hz, 1H), 7.32 (m, 5H); ^{13}C NMR δ 22.4, 23.5, 25.7, 32.6, 48.6, 49.6, 57.3, 68.5, 71.4, 127.5, 128.1, 129.3, 131.7, 138.5, 146.6. Anal. Calcd for $C_{17}H_{18}O$: C, 86.67; H, 7.61. Found: C, 86.73; H, 7.55.

(1*R*,2*R*,3*R*,4*R*,6*S*,7*R*)-8-(Acetoxymethyl)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]non-8-ene (3c) was obtained as a colorless liquid by MPLC (petroleum ether/Et_2O 90/10): yield 53% (99.9% purity by GC); $[\alpha]^{20}_{589}$ +12.8° (*c* 2.0, CH_2Cl_2); retention times (−)-**3c** 23.0 min, (+)-**3c** 23.9 min, ee 78%; IR (neat) ν 3057, 2960, 1742, 1449, 1146 cm^{-1}; ^{1}H NMR δ 1.30 (m, 2H), 1.52 (m, 2H), 1.71 (m, 1H), 2.00 (s, 1H), 2.08 (s, 3H), 2.58 (br s, 2H), 4.67 (d, *J* = 1.3 Hz, 2H), 5.97 (dd, *J* = 1.3, 2.2 Hz, 1H); ^{13}C NMR δ 21.0, 22.6, 23.5, 26.0, 32.8, 48.7, 49.8, 57.5, 63.0, 132.7, 144.5, 170.9. Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.89; H,7.75.

(1*R*,2*R*,3*R*,4*R*,6*S*,7*R*)-8-(Pivaloxymethyl)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]non-8-ene (3d) was obtained as a colorless liquid by MPLC (petroleum ether/Et_2O 90/10): yield 48% (99.7% purity by GC); $[\alpha]^{20}_{589}$ +0.4° (*c* 2.0, $CHCl_3$); retention times (−)-**3d** 54.7 min, (+)-**3d** 56.0 min, ee 32%; IR (neat) ν 3058, 1730, 1625, 1282, 1152 cm^{-1}; ^{1}H NMR δ 1.21 (s, 9H), 1.29 (br s, 1H), 1.32 (br s, 1H), 1.53 (s, 2H), 1.70 (m, 1H), 2.00 (br s, 1H), 2.55 (m, 2H), 4.67 (d, *J* = 1.3 Hz, 2H), 5.95 (dd, *J* = 1.3, 2.8 Hz, 1H); ^{13}C NMR δ 22.0, 23.4, 25.4, 27.3, 32.8, 38.9, 48.6, 49.7, 57.5, 62.9, 132.1, 144.8, 170.9. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 75.35; H, 8.75.

(1*S*,2*R*,3*R*,4*R*,6*S*,7*R*)-8-(Hydroxyethyl)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]non-8-ene (3e) was obtained as a yellow liquid by MPLC (petroleum ether/Et_2O 50/50): yield 58% (99.8% purity by GC); $[\alpha]^{20}_{589}$ +0.4°, $[\alpha]^{20}_{404}$ −20.1° (*c* 2.0 , CH_2Cl_2), ee 95%; IR (neat) ν 3350, 3053, 1615, 1206 cm^{-1}; ^{1}H NMR δ 1.26 (m, 2H), 1.51 (m, 2H), 1.52 (br, OH), 1.70 (m, 1H), 1.95 (br s, 1H), 2.40 (d, *J* = 1.3 Hz, 1H), 2.43 (dt, *J* = 1.3, 6.3 Hz, 2H), 2.55 (br s, 1H), 3.68 (m, 2H), 5.80 (dd, *J* = 1.3, 2.8 Hz, 1H); ^{13}C NMR δ 22.6, 23.7, 25.9, 32.9, 34.6, 48.8, 51.6, 57.5, 60.8, 130.7, 146.5. Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.31; H, 8.85.

(1*S,2*R**,3*R**,4*R**,6*S**,7*R**)-8-(Methoxyethyl)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]non-8-ene (3f)** was obtained as a colorless liquid by MPLC (petroleum ether/Et_2O 90/10): yield 97% (99.9% purity by GC); IR (neat) ν 3053, 1644, 1206, 1053 cm^{-1}; ^{1}H NMR δ 1.25 (m, 2H), 1.49 (m, 2H), 1.66 (m, 1H), 1.92 (br s, 1H), 2.43 (dt, *J* = 1.5, 7.0 Hz, 2H), 2.47 (br s, 1H), 2.50 (s, 1H), 3.34 (s, 3H), 3.47 (t, *J* = 7.0 Hz, 2H), 5.68 (m, 1H); ^{13}C NMR δ 22.4, 23.5, 25.6, 31.5, 32.8, 48.6, 51.8, 57.3, 58.6, 71.8, 128.5, 147.0. Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.33; H, 9.05. Optically active **3f**, obtained by etherification (MeI, NaH, THF, rt, 83%) of alcohol **3e** (95% ee) as for **3i**, displays the same spectroscopic features and $[\alpha]^{20}_{589}$ +8.4° (*c* 2.0, CH_2Cl_2), ee 95%.

(1*S*,2*R*,3*R*,4*R*,6*S*,7*R*)-8-(Acetoxyethyl)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]non-8-ene (3g) was obtained as a colorless liquid by MPLC (petroleum ether/Et_2O 75/25): yield 99% (99.9% purity by GC); $[\alpha]^{20}_{589}$ +5.8° (*c* 2.0, CH_2Cl_2); retention times (−)-**3g** 41.1 min; (+)-**3g** 42.1 min, ee 95%; IR (neat) ν 3055, 2956, 1742, 1457, 1242 cm^{-1}; ^{1}H NMR δ 1.25 (m, 2H), 1.49 (br s, 2H), 1.66 (m, 1H), 1.91 (br s, 1H), 2.04 (s, 3H), 2.47 (m, 2H), 2.50 (dd, *J* = 1.4, 7.2 Hz, 2H), 4.14 (t, *J* = 7.2 Hz, 2H), 5.70 (m, 1H); ^{13}C NMR δ 21.0, 22.4, 23.5, 25.7, 30.4, 32.8, 48.7, 51.7, 57.4, 63.4, 129.4, 145.8, 171.1. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.51; H, 8.02.

(1*R*,2*R*,3*R*,4*R*,6*S*,7*R*)-8-(Methoxymethyl)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]non-8-ene (3i). To a slurry of NaH (0.12 g, 5.04 mmol) in dry THF (5 mL) was added of solution of alcohol **3a** (21% ee) (0.62 g, 4.20 mmol) in dry THF (5 mL). The mixture

was stirred for 3 h, and then a solution of MeI (0.72 g, 5.04 mmol) in dry THF (5 mL) was added. After 12 h, MeOH (3 mL) was added and the solvents were evaporated. The residue was diluted with brine, extracted with ether (3 × 15 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by MPLC (petroleum ether/Et_2O 50/50) to give **3i** (0.61 g, 3.78 mmol) as a pale yellow liquid: yield 90% (99.4% purity by GC); $[\alpha]^{20}_{589}$ +5.7 (*c* 2.0, CH_2Cl_2), ee 21%; IR (neat) ν 3053, 1615, 1206 cm^{-1}; ^1H NMR δ 1.30 (m, 2H), 1.51 (m, 2H), 1.69 (m, 1H), 1.99 (br s, 1H), 2.58 (m, 2H), 3.31 (s, 3H), 3.99 (m, 2H), 5.91 (m, 1H); ^{13}C NMR δ 22.5, 23.6, 25.9, 32.8, 48.7, 49.8, 57.6, 57.8, 71.2, 131.8, 146.8. Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.31; H, 8.79.

(1*S*,2*S*,3*S*,4*S*,6*R*,7*R*,8*R*,9*S*)-8-(Methoxymethyl)tetracyclo-[4.3.0.0^{2,4}.0^{3,7}] nonan-9-ol (5a). A 1 M solution of BH_3:THF in THF (13.9 mL, 13.9 mol) was added to a stirred solution of deltacyclene **3i** (0.75 g, 4.60 mmol) in dry THF (5 mL). After 12 h, the excess borane was carefully neutralized by addition of MeOH, before addition of 3 M NaOH (3 mL) and 30% H_2O_2 (3 mL). The mixture was vigorously stirred at room temperature for 2 h and then concentrated, diluted with brine, and extracted with CH_2Cl_2 (15 mL). The combined extracts were dried (Na_2SO_4) and filtered on a Celite pad. The crude product was purified by MPLC (Et_2O). Alcohols (0.72 g, 4.02 mmol) (ratio **5a/6a** = 85/15) were obtained as a pale yellow liquid: yield 87% (99.8% purity by GC); $[\alpha]^{20}_{589}$ +8.5° (*c* 2.0 , CH_2Cl_2); IR (neat) ν 3400, 3053, 1206, 1053 cm^{-1}; ^1H NMR δ 0.87 (m, 2H), 1.18 (m, 1H), 1.51 (m, 2H), 1.91 (br, OH), 2.03 (m, 2H), 2.15 (m, 2H), 3.38 (s, 3H), 3.49 (d, J = 7.7 Hz, 2H), 3.74 (m, 1H); ^{13}C NMR δ 11.3, 12.8, 15.0, 30.9, 39.4, 44.4, 50.6, 53.3, 58.9, 75.2, 77.0. Anal. Calcd for $C_{11}H_{16}O_2$: C 73.30; H 8.95. Found: C, 73.38; H, 8.94.

(1*S*,2*S*,3*S*,4*S*,6*R*,7*R*,8*S*,9*R*)-8-(Methoxyethyl)tetracyclo-[4.3.0.0^{2,4}.0^{3,7}]nonan-8-ol (5b) was obtained by hydroboration–oxidation of compound **3f** (1.02 g, 6.0 mmol), according the procedure described for compound **3i**, as a colorless liquid by MPLC (petroleum ether/Et_2O 25/75): yield 79% (99.9% purity by GC); $[\alpha]^{20}_{589}$ +40.1 (*c* 2.0, CH_2Cl_2), ee 95%; IR (neat) ν 3390, 3053, 1206, 1053 cm^{-1}; ^1H NMR δ 0.88 (m, 2H), 1.18 (m, 1H), 1.48 (d, J = 11 Hz, 1H), 1.56 (d, J = 11 Hz, 1H), 1.75 (m, 3H), 1.93 (m, 2H), 2.09 (br s, 1H), 2.35 (br, OH), 3.35 (s, 3H), 3.47 (m, 2H), 3.67 (br s, 1H); ^{13}C NMR δ 11.1, 13.1, 14.8, 31.2, 32.1, 39.4, 46.5, 50.4, 50.5, 58.6, 72.4, 79.4. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.12; H, 9.30.

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Supplementary Material Available: Detailed data (COSY and H–C correlation) for compounds **3, 5,** and **6** and copies of ^1H and ^{19}F NMR spectra of Mosher ester derivatives (18 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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